ATHEROSCLEROSIS IN PRIMATES

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THE use of non-human primates in experimental work has the advantage that they are in many respects similar to man. This is particularly important in atherosclerosis research because of a controversy which exists over the relationship between the lesions in man and animals. Also, lesions resembling the early human fatty streak occur in them spontaneously (Fox, 1933, Gilbert and Gillman, 1960, Lindsay and Chaikoff, 1957, McGill, Strong, Holman and Werthessen 1960, Rigg, Finlayson, Symons, Hill and Fiennes, 1960, Finlayson and Simons, 1964).

Although early attempts (Kawamura, 1927, Sperry, Jailer and Engle, 1944, Hueper, 1946) to produce atherosclerosis in primates by feeding cholesterol were unsuccessful, more recently chiefly fibrous lesions said to resemble human atherosclerosis, were produced in monkeys deficient in pyridoxine (Rhinehart and Greenberg, 1949, 1951) and more fatty lesions by diets high in fat and cholesterol and deficient in sulphur containing amino acids (Mann, Andrus, McNally and Stare, 1953). A successful atherogenic regime was also developed by Taylor, Cox, Manalo-Estrella and Southworth, 1962, who were able to produce hypercholesterolaemia and arterial lesions in rhesus monkeys by feeding large amounts of butter and cholesterol. One such animal died of myocardial infarction after 4 yr. on this diet.

In the present work a survey has been made of arterial lesions in baboons many of which had been kept in captivity for a number of years and discarded by two research institutions. Also the aortae from vervet monkeys were examined from animals a few months after capture.

In our experimental work we have used the baboon because this species would seem to offer certain advantages. Besides developing the disease in the wild state they are omnivorous and readily eat diets rich in fat and animal products. Also they are less prone to die from infection which hampered the progress of experimental work in rhesus monkeys (Cox, Taylor, Cox and Counts, 1958). Experiments are described which indicate that arterial lesions can be produced in baboons by feeding diets rich in butter and egg yolk or butter and cholesterol for 18 months, while young control animals on a laboratory stock diet show no similar disease within this period.

METHODS

Study of spontaneous disease

A total of 69 baboons were examined all of the species *Papio cynocephalus*. Some 15 were received from the Medical Research Council Bilharzia Unit, St. Albans; the age of these animals was difficult to determine, but all had been kept in captivity from 6–17 yr. Their diet consisted of laboratory rat cake (Diet No. 41, Bruce and Parkes, 1949) and ½–1 lb. of greens or raw carrots every day. The other 54 were received from the Lister Institute, London; some

had been used for trachoma research and had been kept on a similar diet for 3–12 months after captivity ; most were young animals weighing 3–5 kg. and having an estimated age of 1–2 yr. The aortae were taken from all animals with as much of the common iliac arteries and arteries of the neck as possible. In addition the heart, liver, spleen, kidney, suprarenal, uterus and pancreas were examined. Only the brain from the St. Albans animals was examined. The aortae were opened longitudinally, fixed in 10 per cent formol saline for 24 hr., and stained with a mixture of Sudan III/IV in equal parts of 70 per cent alcohol and acetone (Holman, McGill, Strong and Geer, 1958). The stained aortae were then examined and a record of any positively staining areas was made. Frozen and paraffin sections were cut from aortae at sites of red staining areas and also from adjacent undiseased tissue. Histological examination was carried out using a number of conventional stains including Weigert's resorcin fuchsin method for elastic tissue, Alcian Blue and Hale's dialysed iron method for mucopolysaccharide.

The aortae, heart and lungs of 82 vervet monkeys (*Cercopithicus aethiops*) which had been kept in captivity for an average of 8–9 weeks were obtained from Messrs Pfizer Ltd. Sandwich. They had been fed on rat pellets (Diet 41b) and their drinking water was supplemented by a multi-vitamin preparation and oxytetracycline. Their maturity was estimated from the appearance of the teeth, each animal being described as either "mature" or "immature". Staining and examination of the tissues was carried out as described above.

Study of experimental disease

Animals and diets.—Twelve young baboons (*Papio cynocephalus*), 12–18 months old (Shamrock Farms, Brighton, Sussex), of both sexes, were divided equally into 3 groups and given the diet shown in Table I for 18 months. The 2 experimental atherogenic diets consisted

TABLE 1.—*Design of Experiment and Composition of Diet*

Group	Diet	Composition (per cent)	Fat (per cent)	Cholesterol (per cent)	Fatty acid composition of triglycerides*				
					14 : 0	16 : 0	18 : 0	18 : 1	18 : 2
1	Dried Egg Yolk	15							
	Butter	15	22	0·55	7·2	32·3	12·9	33·2	6·9
	Stock†	70							
2	Cholesterol	2							
	Butter	20	22	2·06	10·3	34·0	18·5	25·5	3·8
	Stock†	78							
3	Stock†	100	2	0·05	2·2	25·6	18·0	24·2	17·1

* The figure before the colon denotes chain length : that after the number of double bonds.

† Stock diet : parts by weight of :—bran 17·4, Sussex ground oats 17·4, ground wheat 17·4, ground maize 8·7, ground barley 8·7, white fish meal 4·8, meat and bone meal 9·6, dried skimmed milk 14, dried yeast 1·2, salt mixture 0·4, and cod liver oil 0·4. One 500 mg. tablet of vitamin C was given weekly.

of the control diet (laboratory rat cake) together with 15 per cent dried egg yolk and 15 per cent butter (Group 1) and 2 per cent cholesterol and 20 per cent butter (Group 2). All diets were made into cubes by a local manufacturer (Biovet Ltd., Willingale, Essex). Examination of the control diet showed that it had a low cholesterol content (*circa* 15 mg per cent) whereas those of the two experimental diets were 0·5 and 2·5 per cent respectively. The control diet also had a low fat content (*circa* 2·5 per cent) and had fatty acids rich in linoleic acid. The fat content of the 2 experimental diets was high (*circa* 20 per cent) and its fatty acid composition was low in linoleic acid. Total daily intake of cholesterol was 1·5–2 g. (0·5 g./kg. body weight) for group 1, and 6–8 g. (2·2 g./kg. body weight) for Group 2.

Pathological examination

Animals were bled regularly from the femoral artery after fasting overnight and tranquilizing with sernylan (Parke Davis Ltd., Moor-Jankowski, 1964). Serum was obtained for lipid and protein estimations. After 18 months on the diets, the animals were killed and the organs and vessels examined histologically.

Biochemical analysis

The following were the determinations and methods used :—

Total cholesterol.—Serum (1 ml.) or liver (250 mg.) was extracted with 20 ml. acetone-alcohol (1 : 1 v/v). To an aliquot of the filtrate (1–2 ml.) acetone-alcohol (1 : 1 v/v) was added up to a volume of 2 ml. Hydrolysis and digitonin precipitation were carried out according to the method of Sperry and Webb (1950). The centrifuged and washed digitonide was then dissolved in 6 ml. ferric chloride-acetic acid solution by heating in a water bath at 80° for 10 min., according to the method of Crawford (1958). Concentrated sulphuric acid (4 ml.) was then added, mixed and the intensity of colour read in a colorimeter (wavelength 560 mμ) after 30 min. according to the method of Zlatkis, Zak and Boyle (1953).

Triglycerides.—Serum lipids and liver extracted with methanol-chloroform (2 : 1 v/v) were separated on silicic acid columns (Malinckrodt) into (*a*) triglycerides and cholesterol, and (*b*) phospholipids according to the method of Handel and Zilversmit (1952). The glycerol was determined in fraction (*a*) using the method of Lambert and Neish (1950).

Phospholipids.—An aliquot from fraction (*b*) described above was analysed for lipid phosphorus according to the method of Allen (1940), and total phospholipid estimated by multiplying by a factor of 25.

Fatty acid composition of serum lipids.—Serum was extracted and the lipids separated by thin layer chromatography and the fatty acid composition of the individual lipids determined by the method of Bowyer, Leat, Howard & Gresham (1963).

Serum lipoproteins.—Paper electrophoresis was carried out as described by Smith (1960). A volume of 50 μl. was applied to filter paper strips 4 cm. wide (Whatman No. 3 MM) and electrophoresis carried out in barbitone buffer (Ph 8·6) for 17 hr. at 200 volts and 1·5 mA/strip. Papers were stained with Fat Red 7B and the dye estimated using an automatic integrating photodensitometer. Serum was also examined by the immunoelectrophoretic technique of Grabar and Williams (1955). Lipoproteins, antibody, precipitation lines were identified by staining with Fat Red 7B or Sudan Black.

RESULTS

Spontaneous disease

Baboons.—Macroscopic aortic lesions were seen in 11 out of 15 baboons, from the Bilharzia Unit at St. Albans, when stained with Sudan ; a summary of the pathological findings is described in Table II. Out of the 54 from the Lister Institute only 2 showed lesions consisting of very faint generalised streaking. It would thus appear that the young baboon (1–2 yr.) does not usually show atherosclerotic lesions.

The lesions when seen in the unstained aorta were slightly raised whitish streaks and were found at sites throughout the whole length of the aorta. These were seen more easily after Sudan staining. Microscopically they consisted of moderate intimal thickening containing collagen and rather thick elastic fibrils (Fig. 1). Intracellular and extracellular globules of sudanophil lipid were present in the surface and in the depths of the lesion but did not constitute a major part of the intimal thickening (Fig. 2). Associated changes in some cases consisted of destruction of the internal elastic lamina and disorganisation of the underlying media. Discrete lesions occurred in the coronary arteries of 2 animals from St. Albans. These were fibroelastic in nature and showed duplication of the internal elastic lamina. The other vessels showed no other atherosclerotic lesions, particularly the cerebral arteries. No other abnormal pathological changes were observed except in those animals from St. Albans infected with schistosomes. These animals had granulomata in the liver or lungs consisting of macrophages with some central eosinophilic polymorphonuclear leucocytes surrounding a schistosome egg.

TABLE II.—*Summary of Pathological Findings in Baboons Kept in Captivity for Over 4 Yr.*

Baboon No.	Approx. age (yr.)	Sex	Macroscopic findings	Microscopic findings
1	15–17	F	Streaking in the arch of the aorta, not extensive	Lipid deposits in the intima. Fibrous thickening of the intima. Disorganisation of media deep to lesion
2	5–6	F	Marked streaking in the thoracic aorta	Slight thickening of the intima.
3	11	M	Area of staining in the arch of the aorta	Fibrous thickening of the intima
4	6	F	No staining or streaking	Slight thickening of the intima
5	5	F	Small stained spots in the upper part of the abdominal aorta	Slight thickening of the intima
6	15–17	F	Much streaking throughout aorta	Much thickening of the intima, which is fibromuscular and contains much fat
7	11	M	Very faint streaking in the thoracic and abdominal aorta	Slightly thickened intima in this area. Also a plaque in a section of the aorta not macroscopically stained
8	6	F	No lesions	Slight thickening of the intima
9	13–15	F	Diffuse staining over the whole length of the aorta	Much intimal thickening which is fibrous and contains fat
10	5	M	No lesions	Intima appears normal
11	5–6	M	Staining at site of ductus scar. Vertical streak in upper abdominal aorta	Well localised lesion. Internal elastic lamina destroyed
12	6	—	No lesions	Spongy thickening of the intima. Internal elastic lamina destroyed
13	6	—	One lesion in upper abdominal aorta	Substantial thickening of the intima in lesion
14	7	—	Streak near scar of ductus arteriosus	Slight thickening of the intima
15	7–8	—	Scar of ductus arteriosus stained. Streaking in upper abdominal aorta	Very little fat shown. Slight intimal thickening

Vervet Monkeys.—Of 82 aortae examined, 32 showed macroscopic sudanophilic lesions. In all but 2 of these, they were situated close to the orifices of the renal, superior mesenteric or coeliac arteries. Most commonly affected was the region of the orifices of the renal arteries (Fig. 3) which was affected in 23 cases compared with a corresponding figure of 12 for the coeliac artery and 11 for the superior mesenteric. The intercostal nearest to the coeliac artery was affected in 5 cases and intercostals in the upper part of the thoracic aorta were affected in 8 cases. In only one of these specimens were the lower and upper intercostals affected together. In 2, the lesions were in the region of the aortic scar of the ductus arteriosus. Six had small lesions in the region of the arch of the aorta, not associated with the scar; 3 had lesions in the lower part of the abdominal aorta not associated with the orifices of vessels.

Lesions were almost always very close to and sometimes on the lip of the vessel orifice and were nearly always caudal to the orifice and slightly lateral or medial. In a few cases the lesions were visible as raised whitish areas prior to staining. The sudanophilic areas varied in size from very minute spots, just visible to the naked eye, to larger lesions up to 2 mm. diameter. 29 out of 61 aortae from mature animals

showed lesions (50 per cent) compared with three out of 21 (15 per cent) for immature animals. Of 3 immature specimens with lesions all showed a small lesion in the region of one renal artery.

There was little correlation between the sex of the animal and the presence of aortic lesions.

Microscopically, the lesion consisted of a thickening of the intima (Fig. 4) and contained more fat than those described for the baboon (Fig. 5). Various histochemical stains showed that the lesion contained acid mucopolysaccharide and collagen (Fig. 6).

Experimental lesions in baboons

Pathology.—Pink barely elevated spots were seen after Sudan staining in all aortae of animals given the atherogenic diets (Groups 1 and 2) but none was seen in control animals. The lesions were often distal to branches in both the thoracic and abdominal aortae and were more conspicuous in those fed egg yolk (Group 1).

On microscopic examination, the aortic lesions were found to be similar to those obtained in the old baboons kept in captivity and described above. Histochemical methods showed they were comprised of collagen, elastin, intracellular and extracellular lipid (Figs. 7, 8, 9). There was a striking resemblance to the so-called human fatty streak. No other arterial lesions were found in the coronary, cerebral, or other arteries examined.

Apart from parasitic infection which was seen in the livers of several animals, the only significant finding was the presence of fat in the periportal liver cells (Fig. 10) in animals given cholesterol (Group 2). None was seen in the control group or those given egg yolk (Group 1).

Serum lipids and lipoproteins.—After 3 months on the experimental diet the serum had a significantly elevated cholesterol and phospholipid concentration which continued to increase for a further 3 months and then remained unchanged (Table III). The cholesterol phospholipid ratio showed a small increase. Values were slightly higher for those animals given cholesterol (Group 2) but most of the values were in the range which is considered normal for man (150–300 mg. per cent).

Paper electrophoretic studies showed that in both experimental groups there was an increase in the β-lipoprotein (Table III). In baboons given the stock diet there was a greater amount of α than β-lipoproteins, but after feeding the athero-

EXPLANATION OF PLATES.

FIG. 1.—Intimal plaque in baboon aorta showing abundant elastic fibres. Weigert's resorcin fuchsin × 56.

FIG. 2.—Globules of lipid both intracellular and extracellular in baboon atherosclerotic plaques. Sudan ×560.

FIG. 3.—Plaque (A) in vervet aorta near orifice of renal artery. Sudan ×2·3.

FIG. 4.—Intimal plaque in aorta of mature vervet monkey. H and E × 56.

FIG. 5.—Plaque in vervet aorta showing sudanophilia. Sudan ×56.

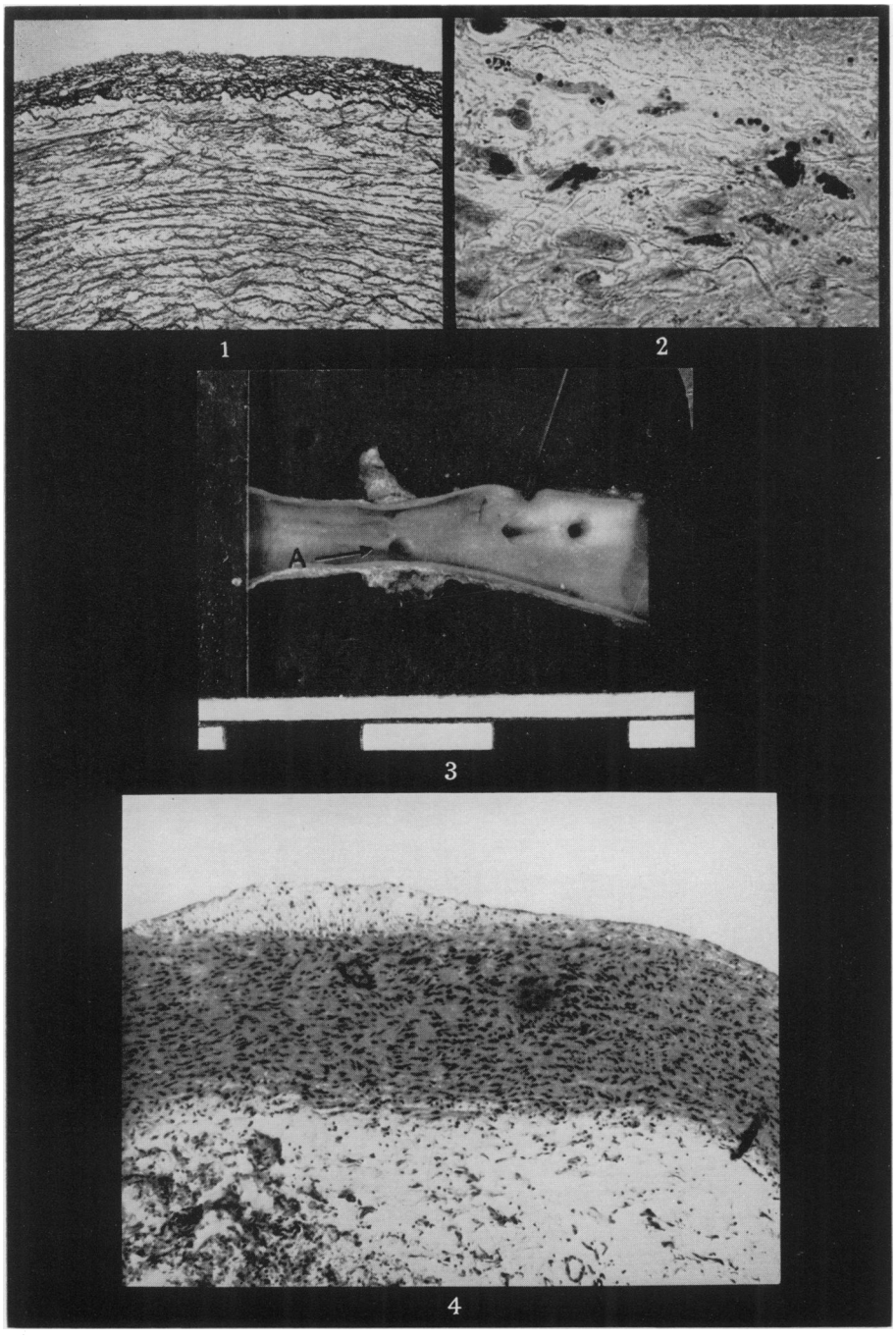
FIG. 6.—Intimal plaque in aorta of mature vervet monkey. Hale's dialysed iron method ×56.

FIG. 7.—Intimal plaque in aorta of baboon fed egg yolk diet (Group 1). H and E ×78.

FIG. 8.—Superficial sudanophil lipid in aortic intimal plaques in baboon fed egg yolk diet (Group 1). Sudan ×70.

FIG. 9.—Diffuse distribution of lipid in intimal plaque of baboons given egg yolk diet (Group 1). Sudan ×70.

FIG. 10.—Lipid in periportal liver cells of animals given cholesterol diets (Group 2). Sudan ×70.



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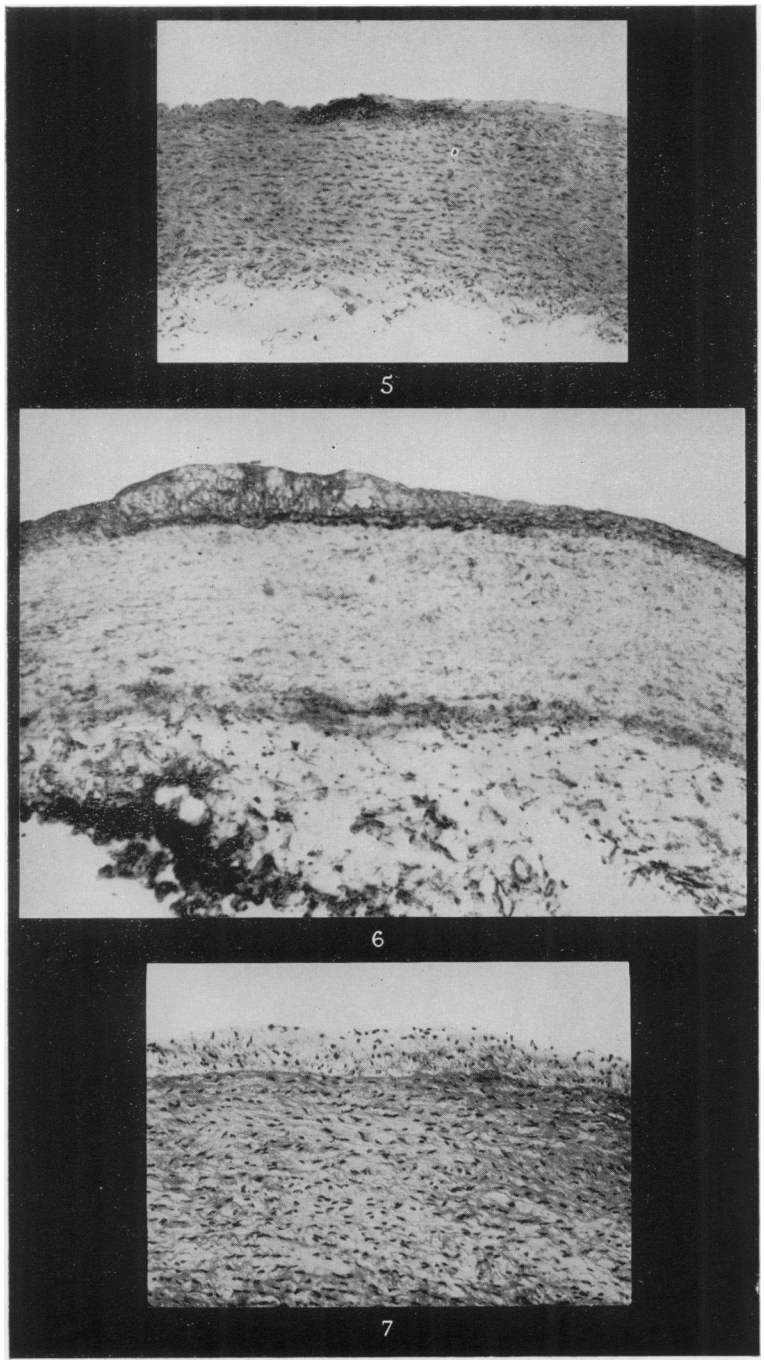

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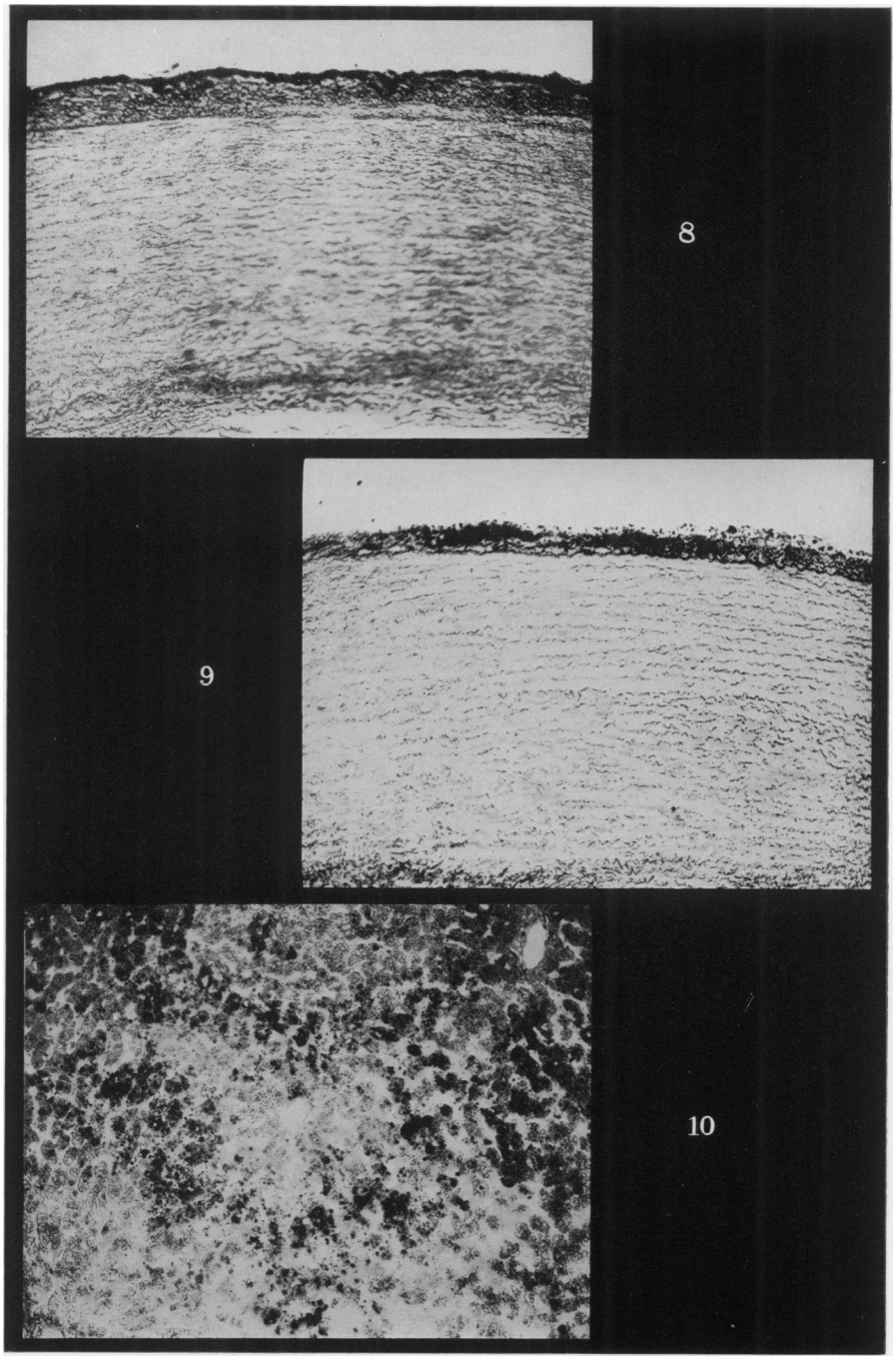

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TABLE III.—*Lipid Analyses of Baboon Serum After Feeding Diets for* 18 *Months**

Group	Diet	Total Cholesterol mg./100 ml.	Tri-glycerides mg./100 ml.	Phospho-lipids mg./100 ml.	Cholesterol Phospho-lipid ratio	Ratio α/β-lipoproteins
1	Egg yolk and butter	204	42·5	326	0·626	0·52
2	Cholesterol and butter	302	41·7	367	0·825	0·59
3	Control	121	46·4	214	0·565	2·00

* Mean of the 4 specimens in each group.

genic diets this pattern was reversed. Human plasma lipoproteins resemble more closely the baboons fed on the atherogenic diet than normal baboons on the control diet. With immunoelectrophoresis the β showed more clearly than the α-lipoproteins, in both control and experimental groups. The greater concentration of β-lipoprotein in the experimental groups could easily be seen and the results confirmed the paper electrophoretic studies.

Serum fatty acid compositions.—The effect of the various diets on the fatty acid composition of the three major serum lipid components, namely, cholesterol esters, triglycerides and lecithin was small (Table IV). In the experimental groups there

TABLE IV.—*Fatty Acid Composition of Individual Lipid Fractions of Sera From Baboons Given the Atherogenic and Control Diets for* 18 *Months*†

	Cholesterol esters Group*			Lecithin Group*			Triglyceride Group*		
Acids*	1	2	3	1	2	3	1	2	3
16 : 0	13·4	14·7	8·9	18·3	23·2	25·5	26·6	26·4	27·1
16 : 1	2·9	3·0	2·5	trace	trace	trace	4·6	4·3	5·8
18 : 0	2·0	3·9	3·0	16·4	20·5	21·2	5·2	5·3	6·0
18 : 1	23·9	26·9	20·6	15·3	12·2	10·4	26·7	31·6	29·7
18 : 2	39·0	40·4	48·0	31·4	28·0	22·2	12·5	10·2	15·5
20 : 4	8·5	3·3	4·8	12·0	6·4	9·0	2·9	0·7	1·7

* Group 1 : 15 per cent egg yolk and 15 per cent butter. Group 2 : 2 per cent cholesterol and 20 per cent butter. Group 3 : control diet.

† Mean of the 4 specimens from each group.

was somewhat less linoleic and more palmitic acid in the cholesterol esters ; however, the lecithin fraction contained more linoleic acid. Triglycerides had decreased linoleic and increased oleic acid. Changes in arachidonic acid were small but animals given egg yolk (Group 1) had increased arachidonic acid levels in all 3 fractions whereas those given cholesterol (Group 2) showed decreases in all fractions.

A comparison was also made with the fatty acid composition from the sera or plasma of other species (Fig. 5). Within each species the fatty acid composition was remarkably uniform for each individual lipid component. Although diet has an influence its effect is usually small. The pattern of fatty acids is remarkably similar in baboon and man and often quite different from that in other species. Thus in the cholesterol esters, baboon serum contains chiefly linoleic acid with oleic acid being the next in importance while the saturated fatty acids are low. In the lecithin fraction, again baboon and man are rather similar, but the comparison between the triglycerides is less striking, in that man contained much less linoleic acid than the normal baboon. Feeding the atherogenic diets to baboons

TABLE V.—*Fatty Acid Composition of Lipids from Various Species**

	Fatty acids				
	Palmitic	Stearic	Oleic	Linoleic	Arachidonic
Cholesterol Esters	16 : 0	18 : 0	18 : 1	18 : 2	20 : 4
Baboon	9	3	21	48	5
Man	10	trace	24	46	6
Pig	7	2	51	31	3
Rabbit	21	trace	23	47	2
Rat	15	8	16	24	30
Lecithin					
Baboon	26	21	10	22	9
Man	28	16	14	25	8
Pig	18	21	29	12	9
Rabbit	24	18	12	36	4
Rat	26	23	9	11	19
Triglycerides					
Baboon	27	6	30	16	1
Man	30	4	45	7	2
Pig	15	6	57	7	1
Rabbit	46	5	21	14	trace
Rat	18	7	44	17	2

* Mean of several normal specimens from fasted animals.

lowers the linoleic content and the triglyceride fatty acid pattern then more closely resembles that of man.

Liver lipids.—As shown in Table VI, baboons given the cholesterol diet (Group 2) had moderately increased liver cholesterol and triglyceride concentrations. Those given the egg diet (Group 1) had normal liver lipids.

TABLE VI.—*Lipid Analyses of Baboon Liver**

Group	Diet	Total Cholesterol mg./100 g.	Triglycerides g./100 g.	Phospholipids g./100 g.
1	Egg yolk and butter	380	1·02	1·75
2	Cholesterol and butter	705	1·89	1·70
3	Control	400	1·17	1·60

* Mean of the 4 specimens in each group.

DISCUSSION

A survey of atherosclerosis in the baboon and vervet monkey has shown that most mature animals have the disease. Thus, 13/15 old baboons and 29/61 mature vervet monkeys showed lesions. An important point is that baboons kept for long periods on laboratory diets can show extensive disease in the aorta. Since the use of primates in experimental work offers such advantages, it is important to establish the extent and severity of disease in control animals as their size precludes the use of large experimental numbers. It is encouraging to note therefore that there is virtually no disease in young animals and the use of the young baboon or vervet monkey in this field recommends itself.

Histologically the lesion seen in non-human primates resembled the early human fatty streak and in addition to lipid contained collagen, elastin and mucopolysaccharides (Gresham and Howard, 1961). In general the vervets' lesions appeared to contain more lipid than the baboons'; and were more localised, affect-

ing chiefly the region of the orifice of the renal artery and to a lesser extent the adjacent vessels. Presumably there is some localising factor at work in this region and not elsewhere. Mechanical factors may be involved since the arteries concerned are the largest branches of the aorta. This may mean that these orifices are the sites in the aorta subject to most mechanical stress. Also there may be differences in metabolism at these points, since differences are known to occur throughout the length of the aorta (Munro and Rifkind, 1964). It is curious that the baboon on the other hand showed no similar localisation of lesions, and streaking occurred throughout the aorta although again these were particularly associated with branching points, the thoracic aorta being most affected.

Initial attempts to produce experimental lesions by feeding atherogenic diets have been most rewarding. After 18 months on two diets, one containing egg yolk and butter and the other 2 per cent cholesterol and butter, atherosclerotic lesions were seen in the aorta which resembled spontaneous lesions and were likewise similar to the early lesions in man. Since young animals were used in this experiment and none of the controls showed any disease it is clear that the changes observed were the result of the dietary regime. None of the experimental animals showed coronary artery lesions and it remains to be seen if similar animals kept for a longer period on the diet could be affected.

The only other notable pathological change was the appearance of moderately fatty livers in the cholesterol fed group. Biochemical analysis showed that the fat in the liver consisted of both cholesterol and triglycerides. It appeared chiefly in the periportal liver cells and the appearance was similar to changes observed in other species fed high fat diets, for instance the rabbit given a semi-synthetic diet containing 20 per cent beef fat (Howard, Gresham, Jones and Jennings, 1964). The failure to find these changes with the egg yolk diet is unexplained but animals in this group have only slightly lower serum cholesterol levels. Also, the high content of phospholipid in egg yolk may prevent the lipid deposition. Human atherosclerosis is not usually associated with the presence of a fatty liver, and feeding of the egg yolk diet would seem to give a closer comparison to the situation in man.

The chief interest in the lipid results is the striking similarity between baboons given atherogenic diets and civilised man. After 3 months on the experimental diet serum cholesterol and phospholipids were elevated and continued to rise over the next few months. The mean levels were in the range considered normal for man. Normal fasted baboons contained chiefly α-lipoproteins rather than β, but this situation was reversed on feeding the atherogenic diet.

Serum triglycerides were not elevated. These are usually increased in patients with coronary heart disease (Schrade, Biegler and Bohler, 1961). However, experimental work in other species suggests that the increase in this lipid may be associated more with the production of thrombosis than atherosclerosis (Howard and Gresham, 1964).

Differences in fatty acid composition of the individual serum lipids were small. Human patients with hyperlipidaemia show a general trend towards a decrease in linoleic and arachidonic acid in preference to the saturated palmitic and stearic acids (Schrade *et al.* 1961). With these diets similar changes were not seen, but the reason for this may be that the elevation of cholesterol and phospholipids was not as large as those in the above human studies. Our observations would suggest that there is little diagnostic value in the determination of serum fatty acid patterns.

The most interesting result was that the fatty acid composition of baboon lipids is remarkably similar to those of man, whereas patterns from other species such as the rabbit, pig, and rat, were often quite different. Cholesterol metabolism is also similar (Kritchevsky, Shapiro and Werthessen, 1962). From both the pathological and biochemical viewpoint the baboon would seem a most useful species for elucidating the aetiology of human atherosclerosis.

SUMMARY

A study has been made of spontaneous arterial disease in the baboon (*Papio cynocephalus*) and vervet monkey (*Cercopithecus aethiops*) and in young baboons given atherogenic diets coutaining 15 per cent egg yolk and 15 per cent butter or 2 per cent cholesterol and 20 per cent butter.

Atherosclerosis was seen in the aortae of old baboons given a laboratory stock diet for 4 yr. and over and in mature recently captured vervet monkeys. Very few young animals showed lesions, and these were sparse.

Histologically the disease resembled the early human fatty streak and consisted of intracellular and extracellular lipid, collagen, elastin and mucopolysaccharide. In the vervets, lesions were localised chiefly at the origins of the renal arteries while in the baboons they were more generalised although more extensive in the abdominal aorta.

Young baboons given the atherogenic diets developed aortic atherosclerosis similar to that seen spontaneously in old animals. Serum cholesterol, phospholipids and β-lipoproteins but not triglycerides were elevated and the values were in the range considered normal for man. Fatty livers were only seen in those animals given the 2 per cent cholesterol diet. The fatty acid compositions of serum-lipids of baboon and man were similar, and unlike those of a number of other species used experimentally.

It is concluded that both from the biochemical and pathological view points, non-human primates may give a closer comparison to man than other species used for atherosclerosis research.

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REFERENCES

ALLEN, R. J. L.—(1940) *Biochem. J.* **34**, 858.

BOWYER, D. E., LEAT, W. M. F., HOWARD, A. N. AND GRESHAM, G. A.—(1963) *Biochim. biophys. Acta*, **70**, 423.

BRUCE, H. M. AND PARKES, A. S.—(1949) *J. Hyg.*, **47**, 202.

COX, G. E., TAYLOR, C. B., COX, L. G. AND COUNTS, M. A.—(1958) *Arch. Path.*, **66**, 32.

CRAWFORD, N.—(1958) *Clin. chim. Acta.*, **3**, 361.

FINLAYSON, R. AND SIMONS, C.—(1964) In 'Biological Aspects of Occlusive Vascular Disease', Ed. Chalmers, D. G. and Gresham, G. A., London (Cambridge University Press), p. 333.

FOX, H.—(1933) In 'Arteriosclerosis'. Ed. Cowdry, E. V., New York (MacMillan).

GILBERT, C. AND GILLMAN, J.—(1960) *S. Afr. J. med. Sci.*, **25**, 59.

GRABAR, P. AND WILLIAMS, C. A.—(1955) *Biochim. biophys. Acta.*, **17**, 67.

GRESHAM, G. A. AND HOWARD, A. N.—(1961) *J. atheroscler. Res.*, **1**, 413.
HANDEL, F. V. AND ZILVERSMIT, D. B.—(1952) *J. Lab. clin. Med.*, **50**, 152.
HOLMAN, R. L., MCGILL, H. C., STRONG, J. P. AND GEER, J. C.—(1958) *Lab. Invest.*, **7**, 4.
HOWARD, A. N. AND GRESHAM, G. A.—(1964) *J. atheroscler. Res.*, **40**, 40.
Iidem, JONES, D. AND JENNINGS, I. W.—(1964). *Proc. Nutr. Soc.* (in Press).
HUEPER, W. C.—(1946) *Amer. J. Path.*, **22**, 1287.
KAWAMURA, R.—(1927) 'Neue Beitrage zur Morphologie und Physiologie der Cholesterinsteatose'. Jena (G. Fischer), p. 267.
KRITCHEVSKY, D., SHAPIRO, I. L. AND WERTHESSEN, N. T.—(1962) *Biochim. biophys. Acta.*, **65**, 556.
LAMBERT, M. AND NEISH, A. C.—(1950) *Canad. J. Res. Sect. B.*, **28**, 83.
LINDSAY, S. AND CHAIKOFF, I. L.—(1957) *Arch. Path.*, **63**, 460.
MANN, G. V., ANDRUS, S. B., MCNALLY, A. AND STARE, F. S.—(1953) *J. exp. Med.*, **98**, 195.
MCGILL, H. C., STRONG, J. P., HOLMAN, R. L. AND WERTHESSEN, M. T.—(1960) *Circ. Res.*, **7**, 234.
MOOR-JANKOWSKI, J.—(1964) in 'The baboon and its use as an experimental animal'. Symposium, San Antonio, Texas, November 1963 (In Press).
MUNRO, A. F. AND RIFKIND, B. M.—(1964) in 'Biological aspects of occlusive vascular disease'. Ed. Chalmers, D. G. and Gresham, G. A., London (Cambridge University Press), p. 50.
RHINEHART, J. F. AND GREENBERG, L. P.—(1949) *Amer. J. Path.*, **25**, 481.—(1951) *Arch. Path.*, **51**, 12.
RIGG, K. J., FINLAYSON, R. SYMONS, C., HILL, K. R. AND FIENNES, R. N. T-W.—(1960) *Proc. zool. Soc. London*, **138**, 157.
SCHRADE, W., BEIGLER, R. AND BOHLE, E.—(1961) *J. Atheroscler. Res.*, **1**, 47.
SMITH, I —(1960) 'Chromatographic and Electrophoretic techniques'. London (Heineman).
SPERRY, W. M., JAILER, J. W. AND ENGLE, E. T.—(1944) *Endocrinol.*, **35**, 38.
Idem AND WEBB, M.—(1950) *J. biol. Chem.*, **187**, 97.
TAYLOR, C. B., COX, G. E., MANALO-ESTRELLA, P. AND SOUTHWORTH, J.—(1962) *Arch. Path.*, **74**, 16.
ZLATKIS, A., ZAK, B. AND BOYLE, A. S.—(1953) *J. Lab. clin. Med.*, **41**, 486.